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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,897	05/14/2001	Andrew D. Hamilton	44574-5100	6169

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EXAMINER

WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

16

DATE MAILED: 02/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/853,897

Applicant(s)

HAMILTON ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice of Non-compliance

DETAILED ACTION

Election/Restrictions

Applicant's election of Group VIII in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Claims

Claims 1-26 have been cancelled in the present amendment.

Claims 29-31 have been added in the present amendment.

Claims 27-31 are under examination.

Specification

The disclosure is objected to because of the following informalities:

A. The specification, e.g., page 27, line 15 up to page 28, line 10 identifies different peptide sequences with Seq. ID. Nos. However, the specification does not contain a separate paper listing of said sequences in the specification and a CRF. The sequences fail to comply with the sequence requirement of 37 CFR 1.821-1.825.

B. The abstract of the disclosure is objected to because of the used of phraseology often used in patent claims e.g., "comprising". Correction is required. See MPEP § 608.01(b).

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The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The method steps of claims 29 and 30 are not supported in the as-filed specification. Applicants point support for claim 29 at page 12, paragraph [0037]. The cited section is different in concept from that of the claim. The disclosure recites

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dissection of a single GFP at the 157 and 158 positions. This results in two GFP fragments to which the peptides are attached at the N-terminus (amino) and C-terminus (carboxy) of the dissected GFP. Therefore, the newly added claims are not describe in the specification.

The specification does not provide adequate written description for the claimed first and second fusion protein. It does not describe how the two separate fusion proteins are fused to the two GFP fragments i.e., at the N or C or mid-part of the GFP. Neither does it describe the kind or size of different proteins from the myriad of known proteins the ones that can be fused to GFP without destroying the function of GFP. Nor has a method by which one determines reassembly of the two proteins is described. The only description provided in the specification deals specifically to a method of reassembly of a specific peptide fragment to form a fusion protein utilizing GFP.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

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out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: step (c), it is not clear as to how the allowing step result in the association of the first and second protein fusion. The steps may result in the association of the first protein with the second GFP or vice versa. It is not clear as to the conditions employ in allowing the reactions to occur. There is a lack of nexus between steps (c) and (d). Step c recites that the allowing step forms the complex of the first and second fusion proteins and step d recites that the reassembly of GFP results in the detection of the two fusion proteins. This claim is inconsistent with the teaching in the disclosure. The disclosure relates to reassembly of peptide fragments to obtain the protein.

B. Claim 28 does not further limit the base claim 27 and broadens the base claim. The base claim does not recite for a nucleic acid. Furthermore, with this step, steps (a) and (b) of the base claim appear redundant. It is unclear, in the context of the claim, how the nucleic acid is obtained.

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C. Claims 29-30 are confusing as to the "dissection" of one GFP fragments from one another. This is inconsistent with the specification teachings, which recite dissecting a single GFP and inserting a peptide fragment to form the NZGFP and CZGFP. Furthermore, this step lacks antecedent basis of support from the base claim, which does not recite for said dissecting step.

D. It is suggested that applicants provide for the full name of the acronyms NGFP and CGFP to avoid any ambiguities.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claim 27 which recites for a method of steps a and b. The specification recites for a peptide fragment of a protein that reassembles to form a protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Michnick et al (WO01/00866) or Mayer (US 2002/0037999) in view of either Anderson et al (6,180,343) or Katz et al (Biotechniques).

Michnick discloses at page 2, lines 1-10 a method by which DHFR was genetically dissected into two rationally designed fragments, each of which can be fused to a library proteins or peptides. Members of one library which heterodimerize with a member of the other library drive the reassembly of the DHFR fragment, resulting in the reconstitution of enzymatic activity.

Mayer discloses at page 4, paragraph [0040], a method comprising of forming a zipper by two WIN-ZIP synthetic amphiphatic segments. The one fusion protein comprises a WIN-ZIP-A1 synthetic amphiphatic segment, and the other fusion protein comprises a WIN-ZIP-B1 synthetic amphiphatic segment. The WIN-ZIP segments preferably interact with each other. In creating one of the fusion proteins, the MPBD of the protein is replaced with a WIN-ZIP-A1 synthetic amphiphatic segment. As such segment contains a short stretch of amino acids, it readily can be substituted for the MPBD without significantly affecting the conformation of the protein. At page 3, paragraph [0023], Mayer suggests the coupling with fluorophores. Each of these references does not disclose coupling with GFP. However,

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Anderson discloses at page 5 fusion proteins comprising a random peptide fused to green fluorescent protein (GFP). It utilizes fusions to the N- and C-termini of GFP comprising presentation structures capable of presenting the peptide in conformationally restricted form. Anderson also discloses fusion of the random peptide to an internal position of GFP, including the loops comprising amino acids 130 to 135, amino acids 154 to 159, amino acids 172 to 175, amino acids 188 to 193, and amino acids 208 to 216. At page 4, Anderson discloses that the fluorescence appears to be a sensitive indication of the preservation of the native structure of the protein, since any disruption of the structure allowing solvent access to the fluorophoric tripeptide will quench the fluorescence.

Katz discloses that GFP is a valuable marker for intracellular protein localization. See the abstract.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the application was made to substitute enzymes with GFP in the fusion proteins of either Mayer or Mischnick in the manner as taught by Katz or Anderson. GFP is known in the art to be a valuable marker for intracellular protein localization of fusion proteins as taught by Katz. And also, for the other advantages taught by Anderson, above. One would have been motivated to use GFP because of its

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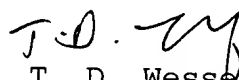
simple structure relative to other identifying markers of fusion proteins such as the enzymes used by Mischnick. Fluorophore detection is at least suggested by Mayer as other means of detection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
February 7, 2003